

PATENT COOPERATION TREATY
PCT
INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)
(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P27879WO Ru/	FOR FURTHER ACTION	
See Form PCT/IPEA/416		
International application No. PCT/EP2004/013649	International filing date (day/month/year) 01.12.2004	Priority date (day/month/year) 02.12.2003
International Patent Classification (IPC) or national classification and IPC A61F2/30, A61L27/56, A61L27/14		
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<ol style="list-style-type: none"> This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36. This REPORT consists of a total of 7 sheets, including this cover sheet. This report is also accompanied by ANNEXES, comprising: <ol style="list-style-type: none"> <input checked="" type="checkbox"/> sent to the applicant and to the International Bureau) a total of 9 sheets, as follows: <ul style="list-style-type: none"> <input checked="" type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions). <input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
<ol style="list-style-type: none"> This report contains indications relating to the following items: <ol style="list-style-type: none"> <input checked="" type="checkbox"/> Box No. I Basis of the opinion <input type="checkbox"/> Box No. II Priority <input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability <input type="checkbox"/> Box No. IV Lack of unity of invention <input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement <input type="checkbox"/> Box No. VI Certain documents cited <input type="checkbox"/> Box No. VII Certain defects in the international application <input type="checkbox"/> Box No. VIII Certain observations on the international application

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**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
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Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
 - This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
 - international search (under Rules 12.3 and 23.1(b))
 - publication of the international application (under Rule 12.4)
 - international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

Description, Pages

1-31 as originally filed

Claims, Numbers

46 as originally filed
1-45 received on 04.10.2005 with letter of 01.09.2005

Drawings, Sheets

1/4-4/4 as originally filed

- a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

- The amendments have resulted in the cancellation of:
 - the description, pages
 - the claims, Nos.
 - the drawings, sheets/figs
 - the sequence listing (*specify*):
 - any table(s) related to sequence listing (*specify*):
- This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
 - the description, pages
 - the claims, Nos.
 - the drawings, sheets/figs
 - the sequence listing (*specify*):
 - any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
 - the entire international application,
 - claims Nos. 44,45
 - because:
 - the said international application, or the said claims Nos. 44,45 relate to the following subject matter which does not require an international preliminary examination (specify):
see separate sheet
 - the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
 - the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
 - no international search report has been established for the said claims Nos. 44,45
 - the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form has not been furnished
 does not comply with the standard
 - the computer readable form has not been furnished
 does not comply with the standard
 - the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
 - See separate sheet for further details

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2-43
	No:	Claims	1
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-43
Industrial applicability (IA)	Yes:	Claims	1-43
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

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Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 44 and 45 relate to subject matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to novelty, inventive step and industrial applicability (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

- D1: EP-A-1 064 958 (ETHICON INC) 3 January 2001 (2001-01-03)
D2: I. AP GWYNN, S. WADE, K. ITO AND R.G. RICHARDS: "Novel aspects to the structure of rabbit articular cartilage." EUROPEAN CELLS AND MATERIALS, vol. 4, 2002, pages 18-29, XP002282963 ISSN 1473-2262

1 INDEPENDENT CLAIM

1.1 The subject-matter of claim 1 is not new in the sense of Article 33(2) PCT, and therefore the criteria of Article 33(1) PCT are not met.

The document D1 discloses (the references in parentheses applying to this document):

A triphasic prosthetic device for repairing or replacing cartilage or cartilage like-tissue (paragraph 28-30) comprising:

- a polymeric hollow body component (paragraph 30, lines 23-26) with a number of highly oriented hollow bodies;
- a base component (paragraph 30, lines 26-28) to anchor said polymeric hollow body component (paragraph 30, lines 23-26) in or onto an osteochondral

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environment and

- at least one superficial layer comprising randomly oriented fibres (paragraph 29, lines 3-5; paragraph 30, lines 15-18) provided on said polymeric hollow body component (paragraph 30, lines 23-26)

wherein said number of highly oriented hollow bodies of the polymeric hollow body component (paragraph 30, lines 23-26 and figure 8) are aligned perpendicularly to the plane of the articulating surface to more than 50% (paragraph 30, lines 25 and 26).

The subject-matter of claim 1 is therefore not new (Article 33(1) and (2) PCT).

2 DEPENDENT CLAIMS

2.1 According to the teachings of D1 a **triphasic prosthesis device** resembles the natural structure of articular cartilage (see D1, Paragraph 28-30 in this respect). The knowledge regarding the structure of natural cartilage at the time of publication of D1 is illustrated by figure 8 of D1. However, according to D2, further details with regard to the structure of the natural cartilage has been obtained. See in particular D2, abstract, last sentence and figure 1. It would therefore be natural for the person skilled in the art to apply this new knowledge the **triphasic prosthesis device** known from D1, thereby arriving at **triphasic prosthesis device** according to claims 2-43.

In view of paragraph 3 above, the skilled person would regard it a normal design procedure to combine all the features set out in claims 2-43. Thus, the subject-matter of claims 2-44 does not involve an inventive step and does not satisfy the criterion set forth in Articles 33(1) and 33(3) PCT.

3 It is furthermore noted:

3.1 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1 and D2 are not mentioned in the description, nor are these documents identified therein.

3.2 The description is not in conformity with the claims as required by Rule 5.1(a)(iii) PCT.

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3.3 Independent claim 1 is not in the two-part form in accordance with Rule 6.3(b) PCT, which in the present case would be appropriate, with those features known in combination from the prior art (document D1) being placed in the preamble (Rule 6.3(b)(I) PCT) and with the remaining features being included in the characterising part (Rule 6.3(b)(ii) PCT).

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New Claims

1. A triphasic prosthetic device for repairing or replacing cartilage or cartilage like-tissue (1)
10 comprising
 - a polymeric hollow body component (3) with a number of highly oriented hollow bodies;
 - a base component (4) to anchor said polymeric hollow body component (3) in or onto an osteochondral environment and
 - at least one superficial layer comprising randomly oriented fibres (2) provided on said polymeric hollow body component (3)wherein said number of highly oriented hollow bodies of the polymeric hollow body component (3) are aligned perpendicularly to the plane of the articulating surface to more than 50%.

2. The device according to claim 1,

- 25 wherein said hollow bodies are aligned to more than 90 %, preferably more than 95 %.

3. The device according to at least one of claims 1 or 2,
wherein the inner channel diameter of the hollow
bodies of polymeric hollow body component (3) is in a
range of 500 nm to 500 μm .

5

4. The device according to claim 3,
wherein said inner channel diameter is in a range of 5
 μm to 150 μm .

10

5. The device according to at least one of claims 1 to 4,
wherein the polymeric hollow body component (3) is
formed by an assembly of oriented tubes.

15

6. The device according to claim 5,
wherein the space between the assembled tubes is empty
or filled with a substance selected from the group
consisting of synthetic polymers, natural polymers,
biologically engineered polymers, the molecules
thereof, biomacromolecules and any combination
thereof.

20

7. The device according to at least one of claims 3 to 6,
wherein the channels have a wall thickness ranging
between 1 nm and 500 μm .

25

3

8. The device according to claim 7,

wherein the wall thickness is between 100 nm and 250
μm.

5 9. The device according to at least one of claims 1 to 8,
wherein the hollow body component is a solid block of
polymer with channels.

10. The device according to at least one of claims 3 to 9,
10 wherein the channels are formed by mechanical,
physical and/or chemical methods in a solid polymer.

11. The device according to at least one of the claims 1
to 10,
15 wherein said solid polymer is porous.

12. The device according to at least one of claims 1 to
11,
wherein the lateral distribution of the hollow bodies
20 of component (3) is homogenous, random or in an
specific pattern.

13. The device according to at least one of claims 1 to
12,
25 wherein said hollow bodies of the hollow body
component (3) have a height of 50 μm to 10 mm.

14. The device according to claim 13,

wherein the height is between 100 µm to 2 mm.

15. The device according to at least one of claims 1 to

5 14,

wherein the fibers of the superficial layer (2) comprise a material selected from the group consisting of synthetic polymers, natural polymers, biologically engineered polymers, the molecules thereof,

10 biomacromolecules and any combination thereof.

16. The device according to at least one of claims 1 to

15,

wherein the base component (4) comprises a bone
15 substitute material.

17. The device according to claim 16,

wherein said bone substitute is a material selected from the group consisting of synthetic polymers,

20 natural polymers, biologically engineered polymers, the molecules thereof, biomacromolecules and any combination thereof.

18. The device according to claim 16,

25 wherein said bone substitute is a mineral material.

19. The device according to claim 18,

wherein said material is a synthetic ceramic.

20. The device according to claim 19,
wherein said a synthetic ceramic comprises at least
one of calcium phosphate, calcium sulfate and calcium
5 carbonate.

21. The device according to claim 20,
wherein said calcium phosphate is selected from the
group consisting of dicalcium phosphate dihydrate
10 ($\text{CaHPO}_4 \times 2\text{H}_2\text{O}$), dicalcium phosphate (CaHPO_4), alpha-
tricalcium phosphate (alpha- $\text{Ca}_3(\text{PO}_4)_2$), beta-tricalcium
phosphate (beta- $\text{Ca}_3(\text{PO}_4)_2$), calcium deficient hydroxyl
apatite ($\text{Ca}_9(\text{PO}_4)_5(\text{HPO}_4)\text{OH}$), hydroxyl apatite
15 ($\text{Ca}_{10}(\text{PO}_4)_6\text{OH}_2$), carbonated apatite
($\text{Ca}_{10}(\text{PO}_4)_3(\text{CO}_3)_3(\text{OH})_2$), fluoroapatite
($\text{Ca}_{10}(\text{PO}_4)_6(\text{F},\text{OH})_2$), chloroapatite ($\text{Ca}_{10}(\text{PO}_4)_6(\text{Cl},\text{OH})_2$),
whitlockite (($\text{Ca},\text{Mg})_3(\text{PO}_4)_2$), tetracalcium phosphate
20 ($\text{Ca}_4(\text{PO}_4)_2\text{O}$), oxyapatite ($\text{Ca}_{10}(\text{PO}_4)_6\text{O}$), beta-calcium
pyrophosphate (beta- $\text{Ca}_2(\text{P}_2\text{O}_7)$), alpha-calcium
pyrophosphate, gama-calcium pyrophosphate, octacalcium
phosphate ($\text{Ca}_8\text{H}_2(\text{PO}_4)_6 \times 5\text{H}_2\text{O}$) and mixtures thereof.

22. The device according to claim 19,

wherein said synthetic ceramic comprises metallic,
25 semimetallic components and/or non-metallic
components, preferably magnesium, silicon, sodium,
potassium, strontium and/or lithium.

23. The device according to any of the claims 17 to 22,
wherein the material is a composite material
comprising at least two different components.

5

24. The device according to any of claims 16 to 23,
wherein the bone substitute material is highly porous
with interconnecting pores.

10 25. The device according to any of claims 17 to 24,
wherein the shape of the base component (4) is round
cylindrical or conical.

15 26. The device according to claim 25,
wherein the diameter of the base component (4) ranges
between 4 and 20 mm, with a height being 1 to 30 mm.

20 27. The device according to claim 26,
wherein the diameter of the base component (4) ranges
between 4 and 20 mm, with a height being between 1 to
10 mm.

25 28. The device according to at least of claims 1 to 27,
wherein said superficial layer (2) has a thickness of
1 nm to 5 mm.

29. The device according to claim 28,

wherein said thickness is in the range of 10 µm to
2 mm.

5 30. The device according to claim 28 and 29,

wherein said superficial layer (2) is missing, or
formed by uppermost end of the hollow body component.

31. The device according to at least one of claims 1 to

10 30,

wherein at least one of components (2), (3) and (4)
has a liquid absorbing capacity in a range of 0.1 % to
99.9 %.

15 32. The device according to claim 31, wherein said liquid
absorbing capacity is in a range of 20.0 to 95.0 %.

33. The device according to claim 31 or 32,

20 wherein the liquid is an aqueous media and/or a body
fluid.

34. The device according to at least one of the preceding
claims,

wherein the polymeric components are cross-linked.

25

35. The device according to at least one of preceding
claims further comprising at least one externally
added component.

36. The device according to claim 35,
wherein said components are cells of different origin.

5 37. The device according to claim 36,
wherein said cells are autologous cells, allogenicous
cells, xenogenous cells, transfected cells and/or
genetically engineered cells.

10 38. The device according to claim 35, 36 or 37,
wherein chondrocytes, chondral progenitor cells,
pluripotent cells, tutipotent cells or combinations
thereof are present throughout the components (2)
and/or (3).

15

39. The device according to claim 35, 36 or 37,
wherein osteoplasts, osteo-progenitor cells,
pluripotent stem cells, tutipotent stem cells or
combinations thereof are present throughout the base
20 component (4).

40. The device according to claim 35, 36 or 37,
wherein blood or any fraction thereof is present
throughout the base component (4).

25

41. The device according to claim 35,
wherein pharmaceutical compounds are contained.

42. A device according to at least one of the preceding claims,

5 wherein a cell barrier layer is additionally provided between said polymeric hollow body component (3) and said base component (4).

43. A device according to claim 42,

10 wherein the cell barrier layer is a cell selective barrier layer.

44. A use of the device according to at least one of the preceding claims for implantation in articulating joints in humans and animals.

15

45. The use according to claim 44 for regeneration of articulator cartilagenous tissue.